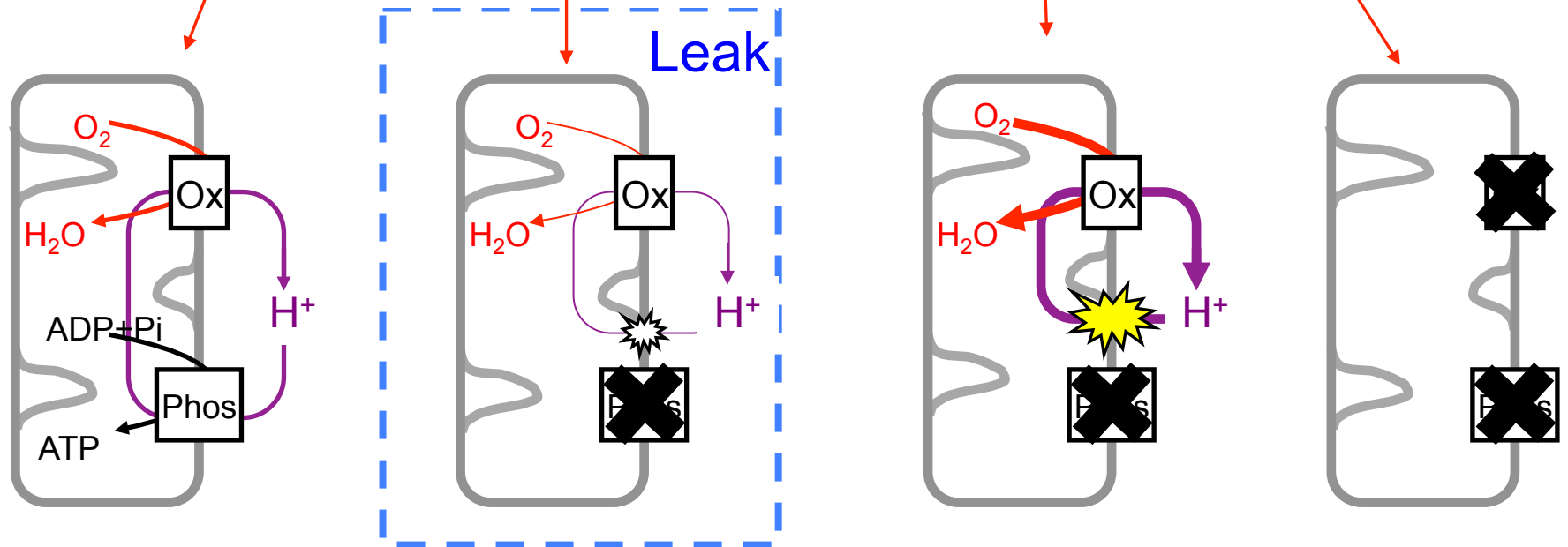
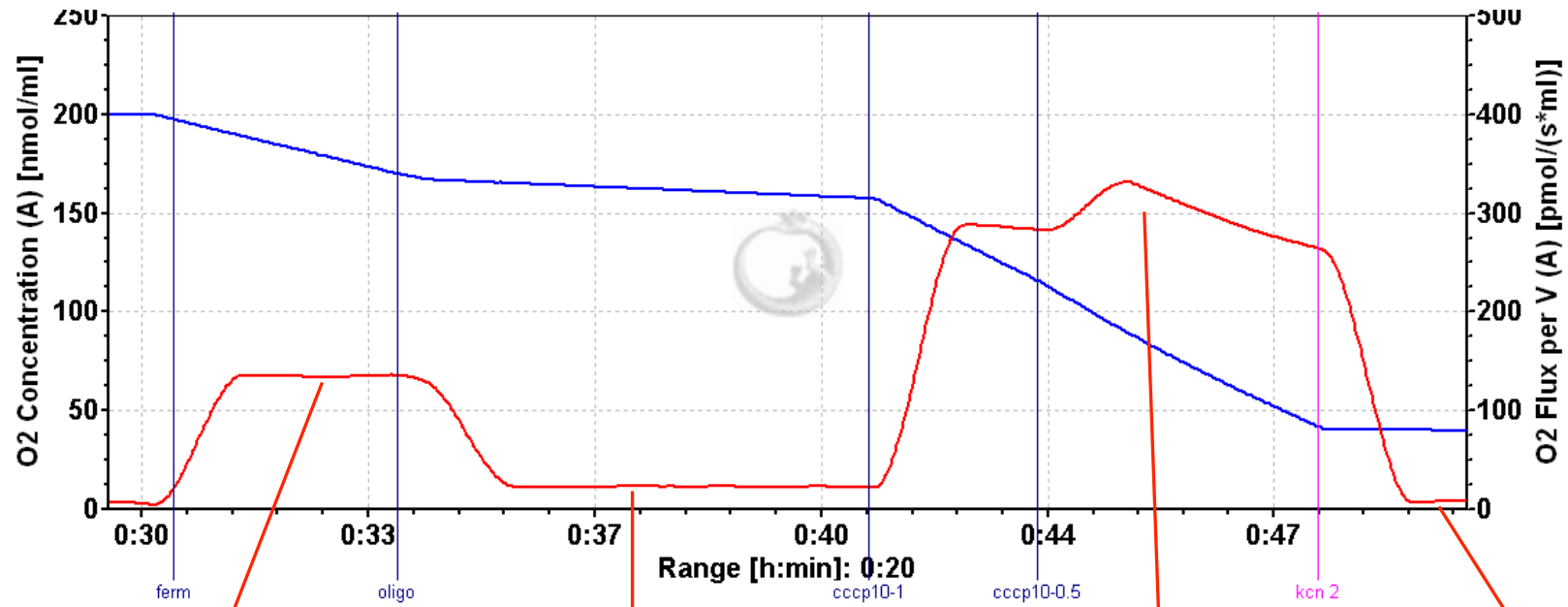
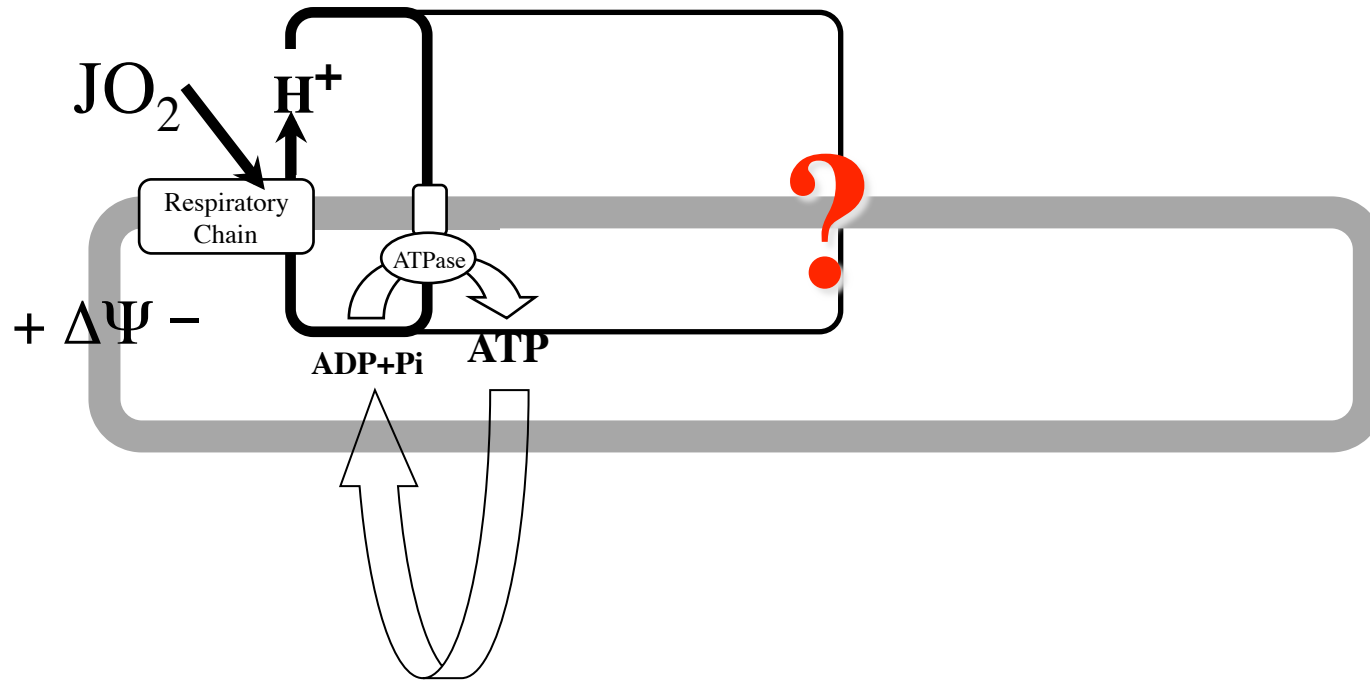


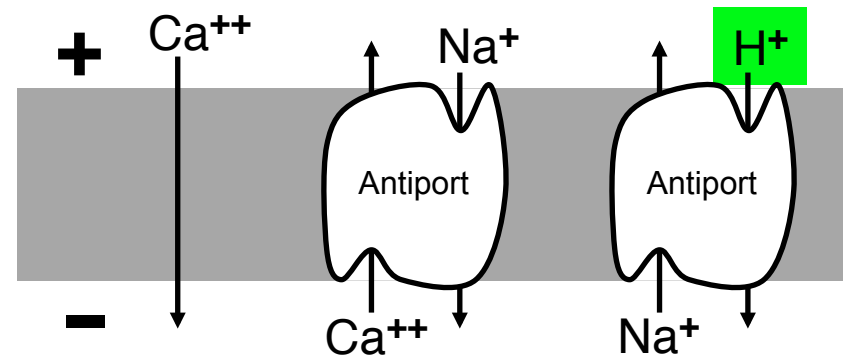
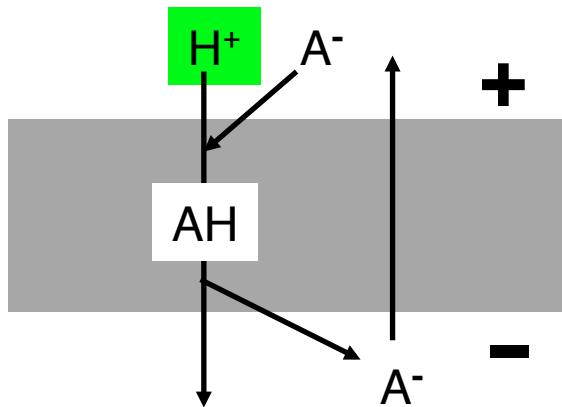
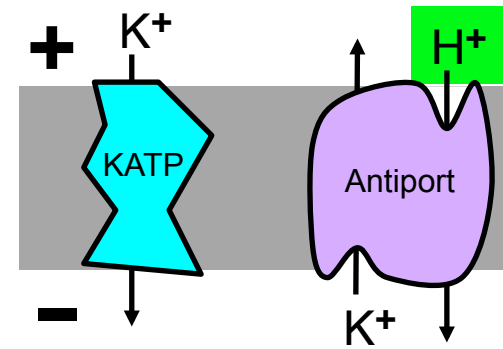
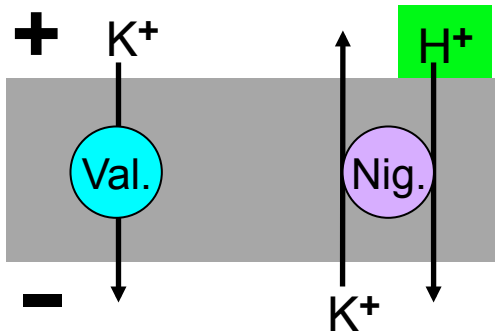
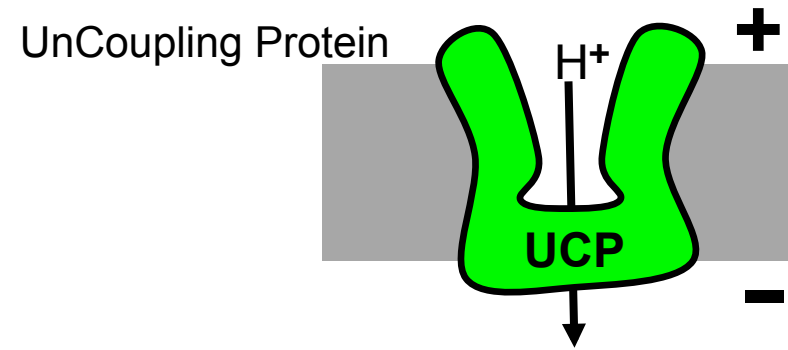
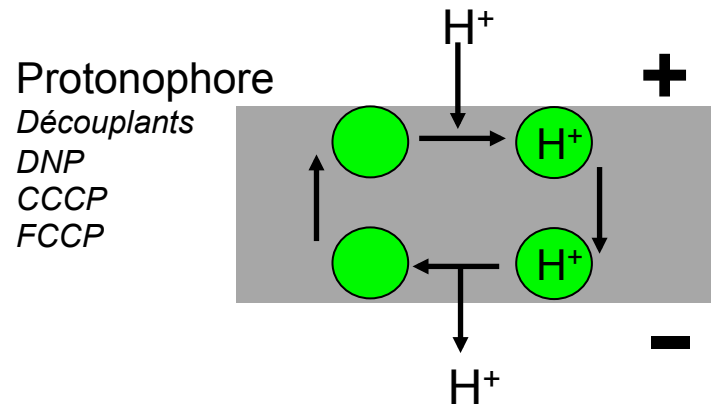
1) L'état non phosphorylant et la fuite de protons mitochondriale

Proton leak = oligomycin rate (intact cells)



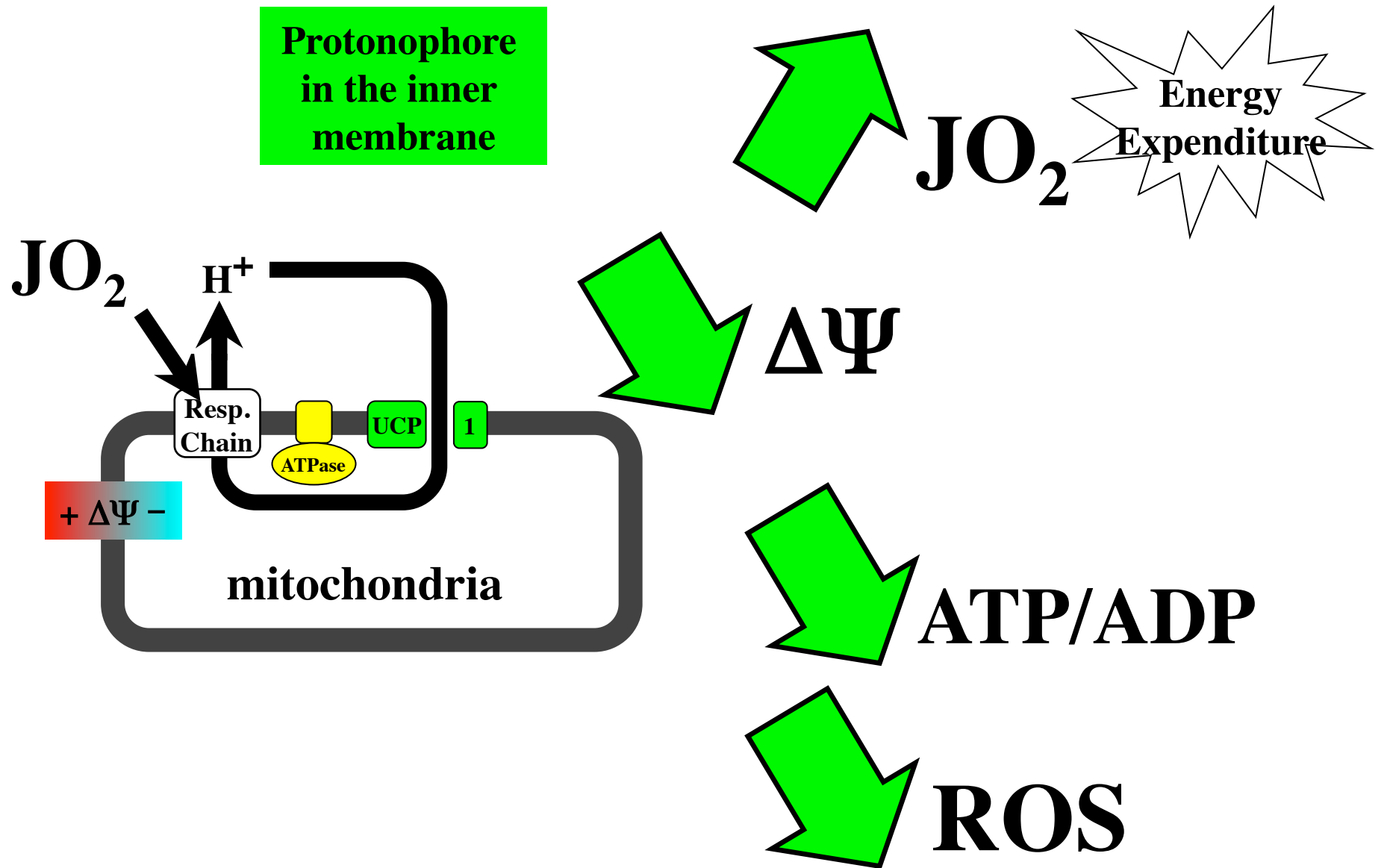


Transport de protons effet direct ou indirect

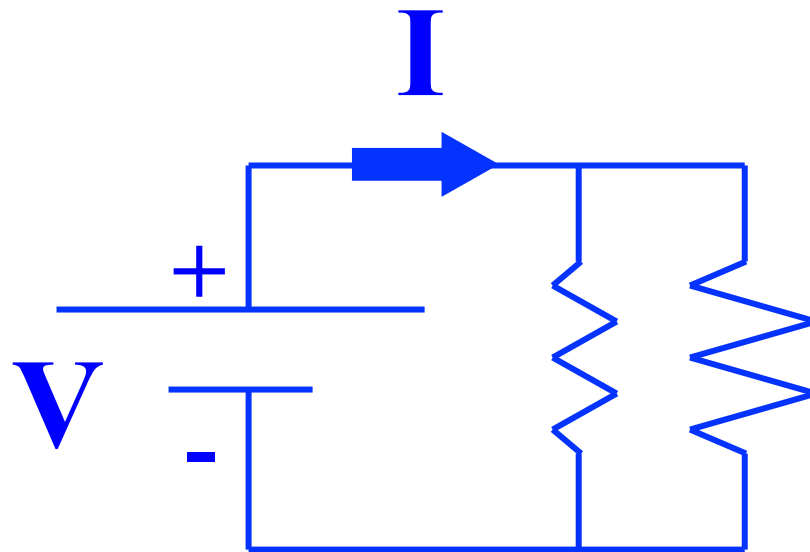
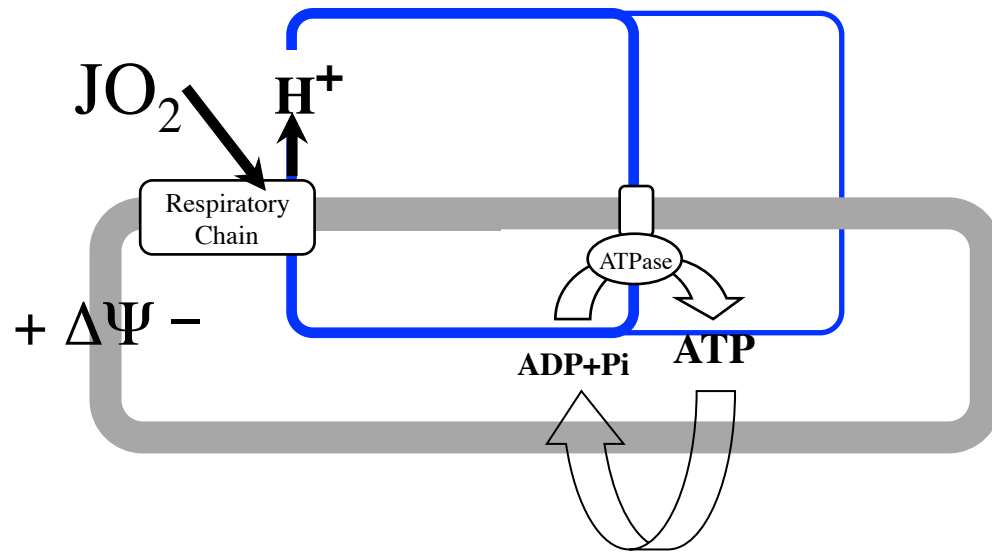


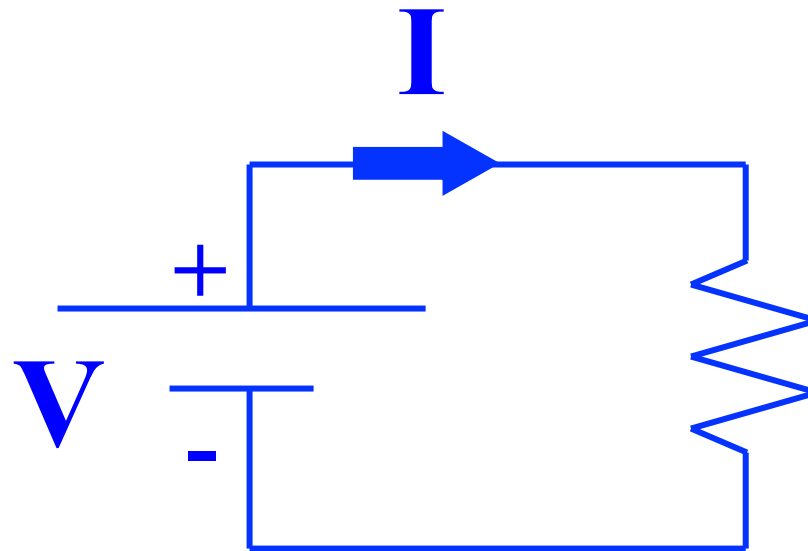
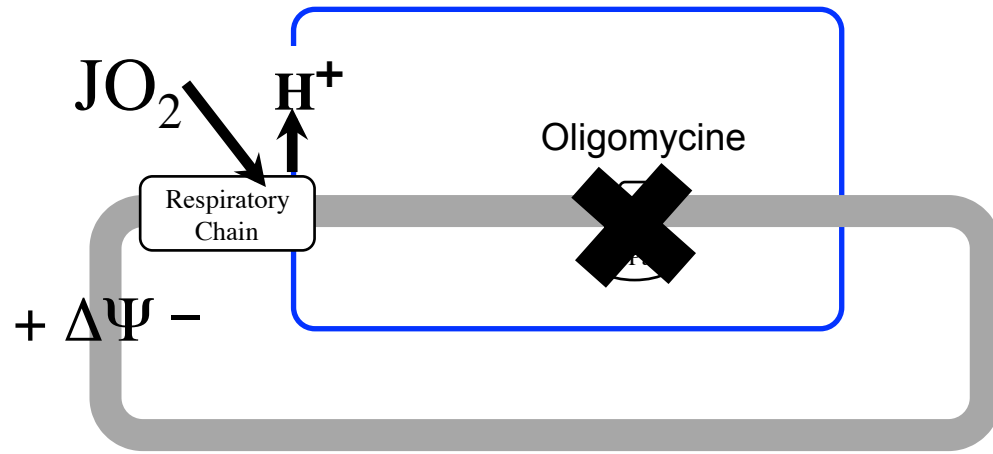
La fuite apparaît régulée

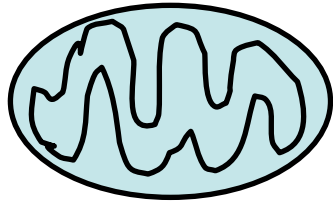
- Suit le métabolisme de base
 - Etat thyroïdien
 - Taille des mammifères (oiseaux)
 - Reptile/mammifère
 - Corrélation fuite composition PL
- |
— *Martin D Brand*
- Mécanisme thermogénique du Tissu Adipeux Brun
 - Hibernants, adaptation au froid, nouveaux nés, DIT
 - Perméabilité exceptionnelle des mitochondries de TAB
 - Présence d'UCP1
 - Les nouvelles UCPs



2) Caractériser, mesurer la fuite.





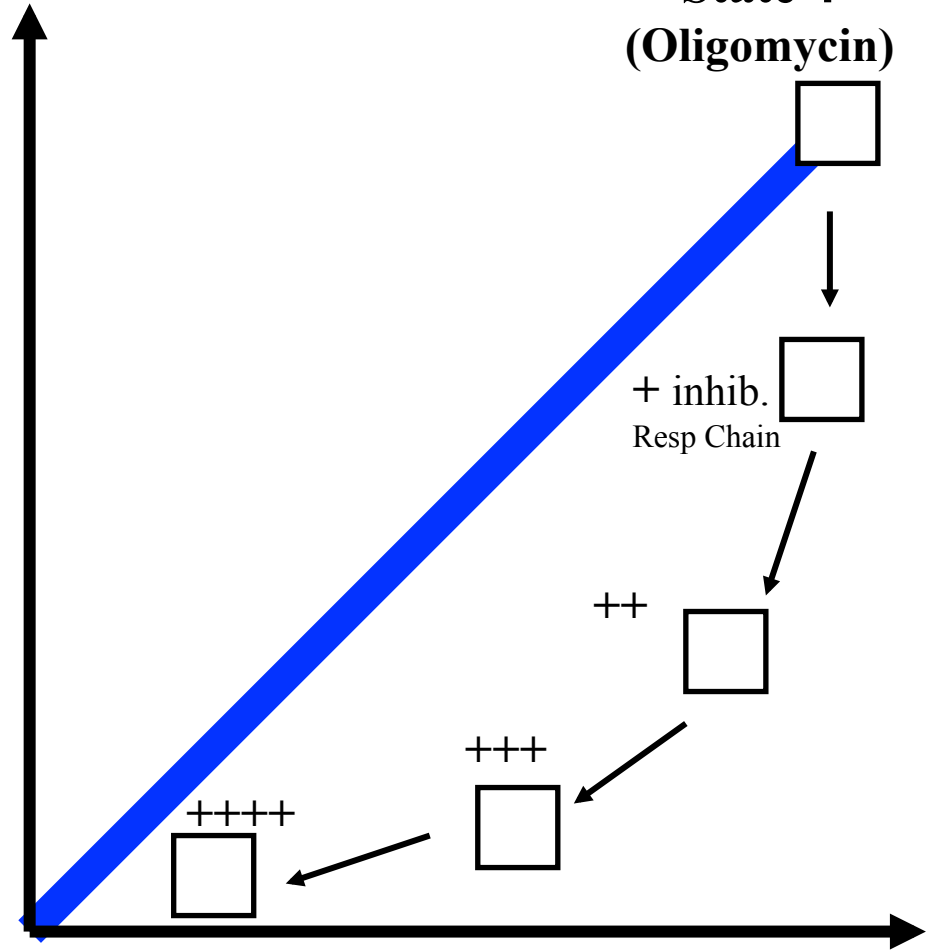


Oxygen consumption

Proton flux

$$V=RI$$

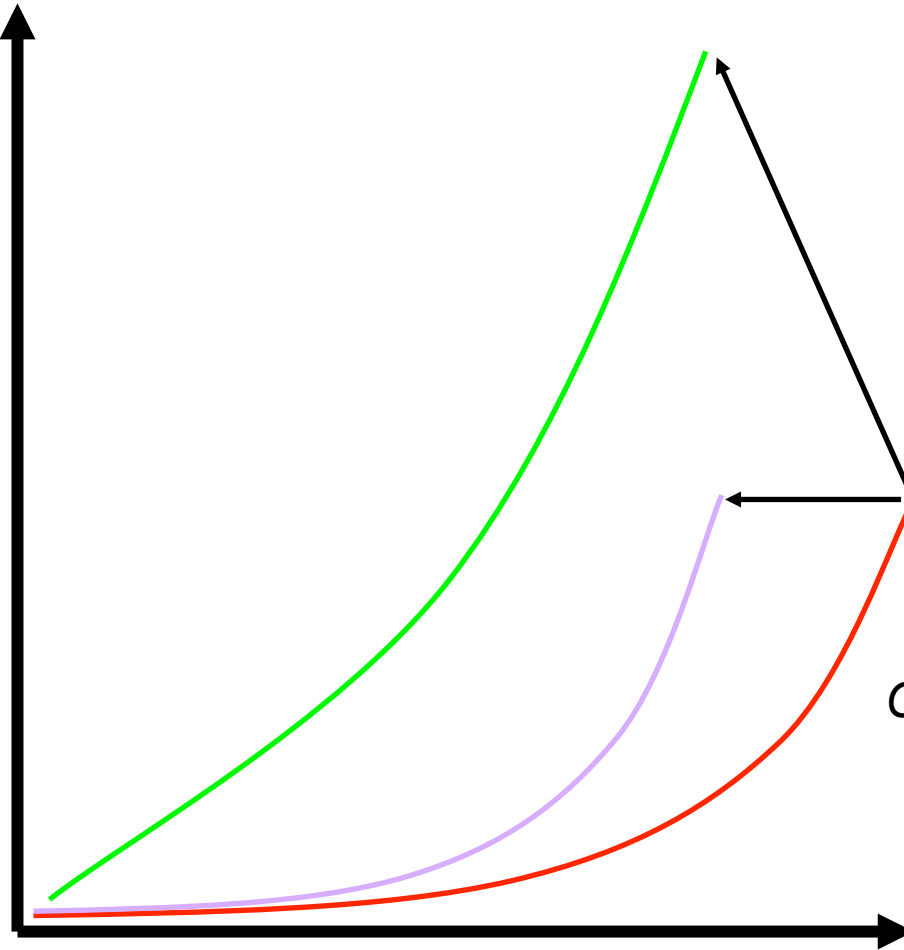
**State 4
(Oligomycin)**



$\Delta\Psi$ (mV)

Respiration rate

Proton flux

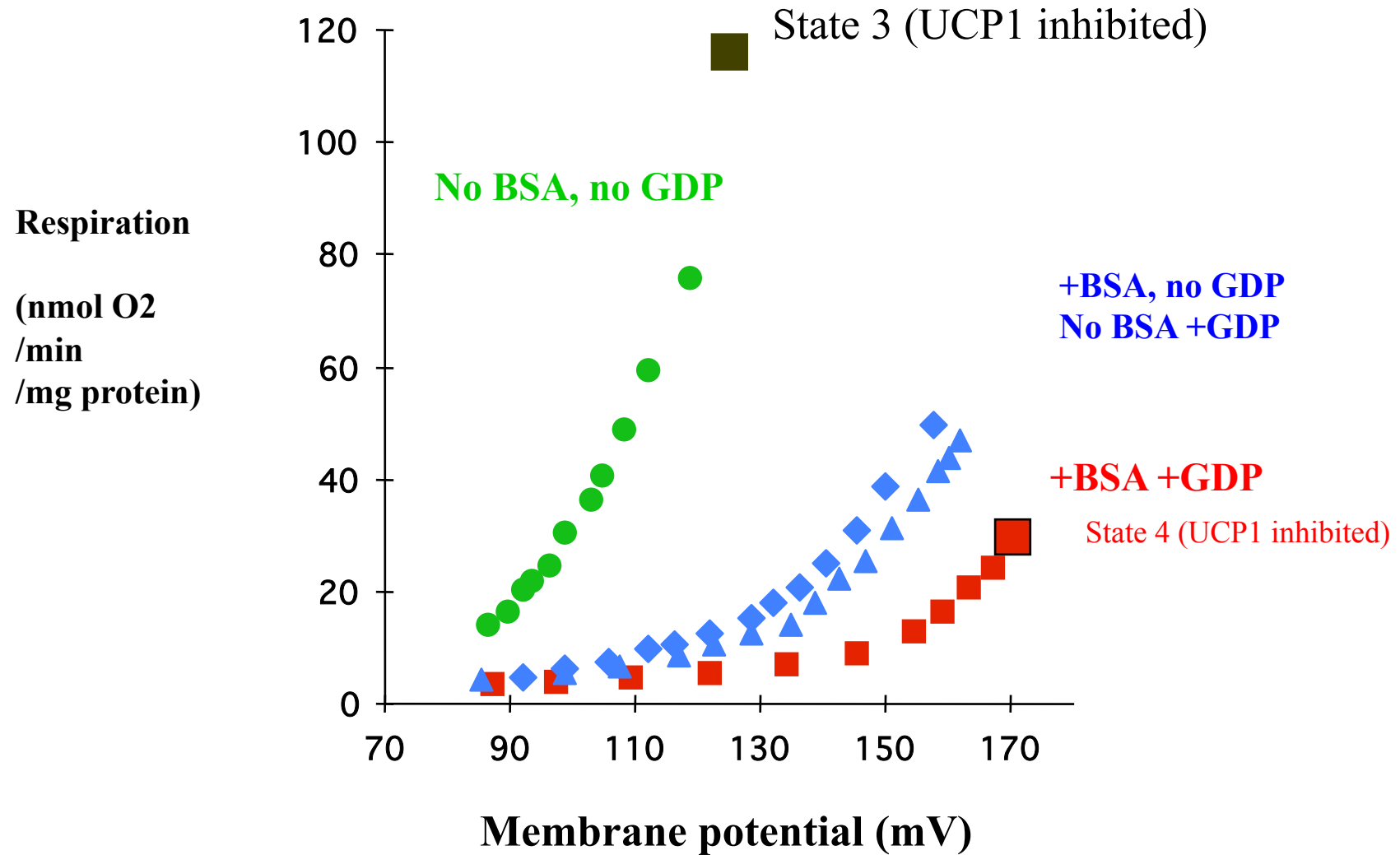


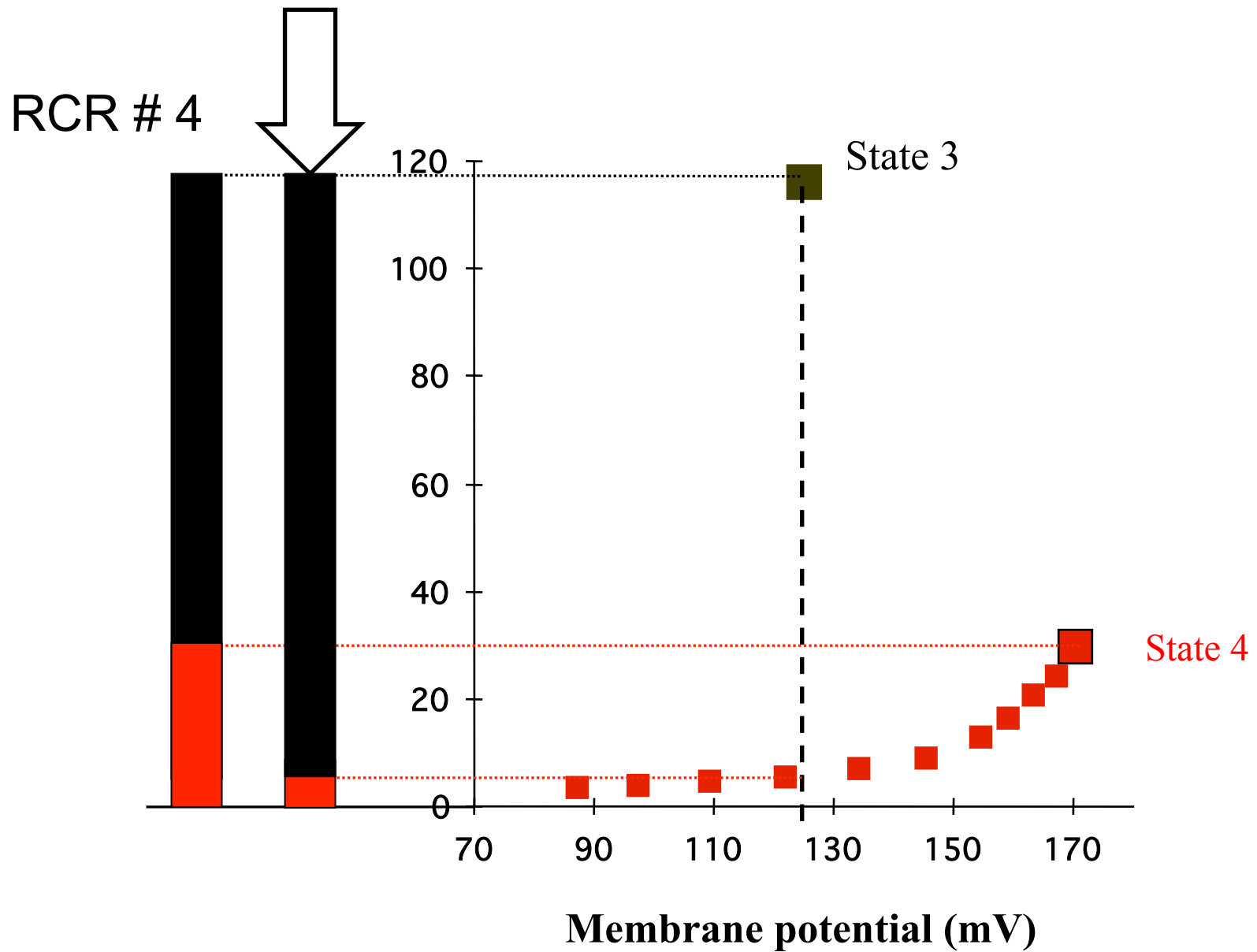
Courbe de Nicholls

$\Delta\Psi$ (mV)

Expression of UCP1 in muscle and heart

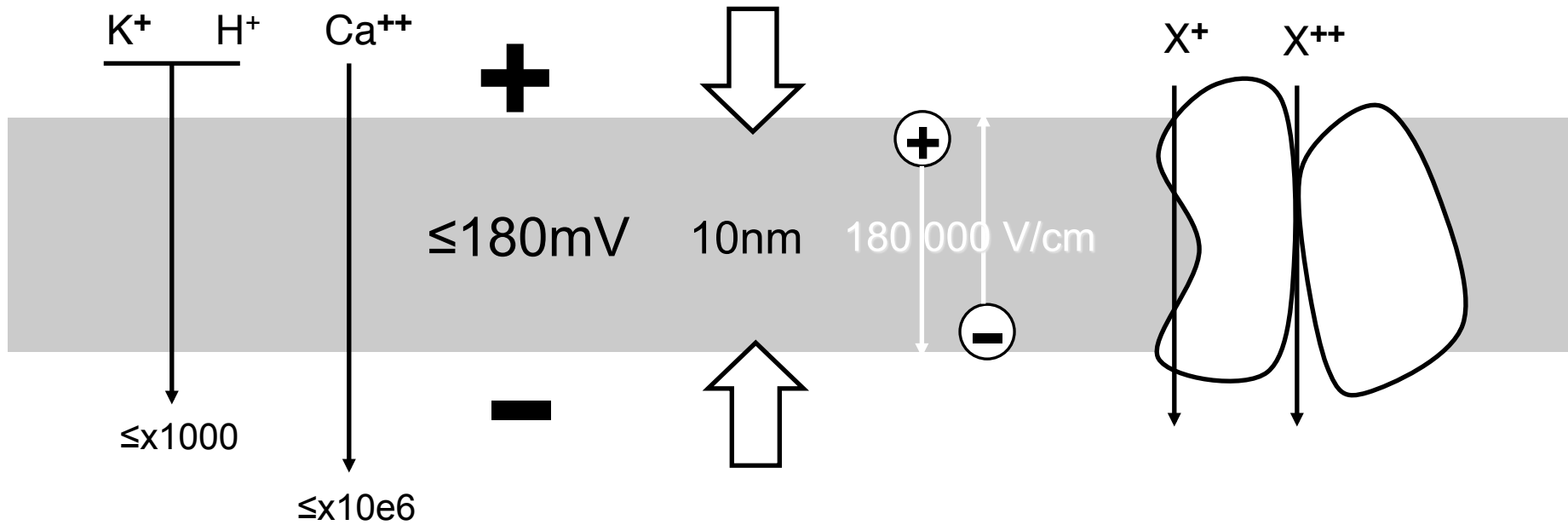
Adapted from Couplan et al. (2002) J. Biol. Chem.





Tout près de la limite...

$$mV = \frac{RT}{zF} \log\left(\frac{C_{\text{ext}}}{C_{\text{int}}}\right)$$



2) Une protéine de fuite: la protéine
déchouplante UCP1

UCP1 et TAB (Cannon & Nedergaard 2004 Physiol rev)

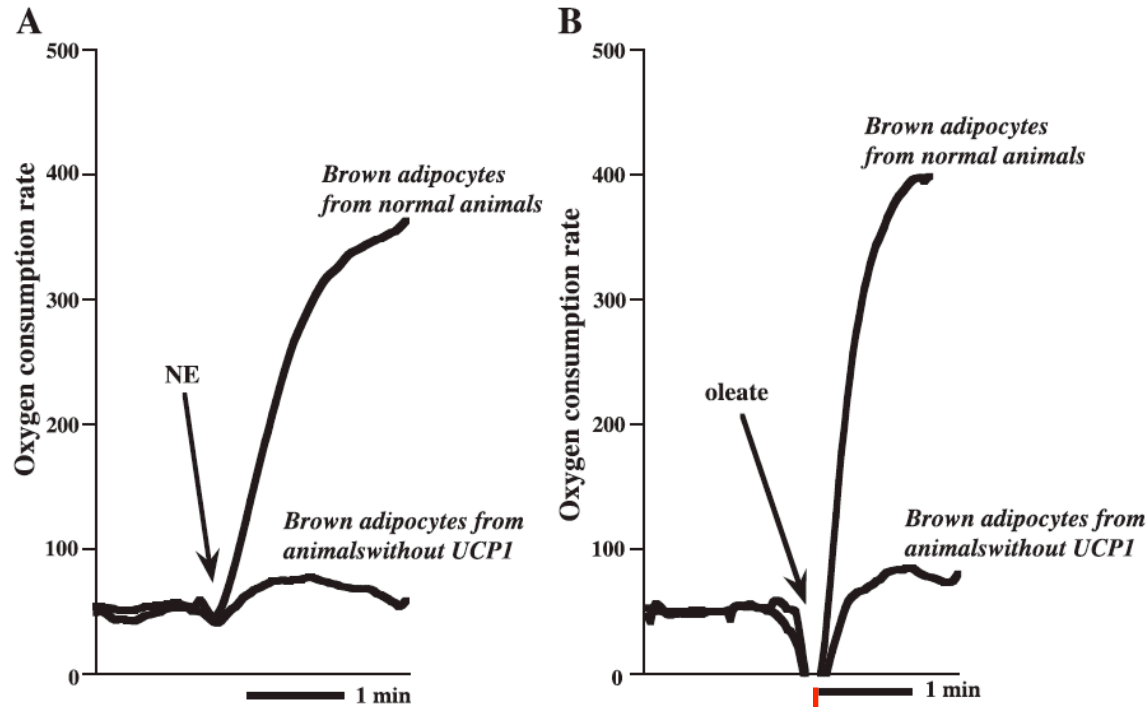
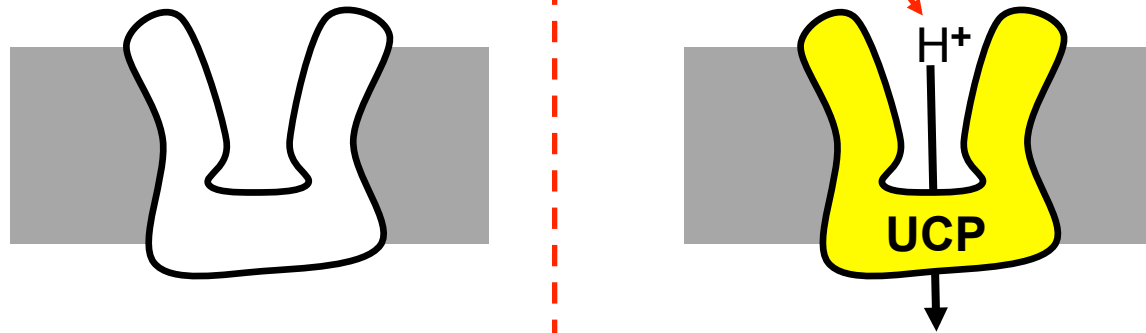


FIG. 3. The unique ability of brown adipocytes to respond to norepinephrine (A) or fatty acid (B) addition with a nearly 10-fold increase in the rate of oxygen consumption (thermogenesis) is fully dependent on the presence of UCP1. Oxygen consumption rates are in $\text{fmol O}_2 \cdot \text{min}^{-1} \cdot \text{cell}^{-1}$ (the apparent, minor responses occurring in brown adipocytes from UCP1-ablated mice are mainly addition artefacts). [Data adapted from Matthias et al. (491).]

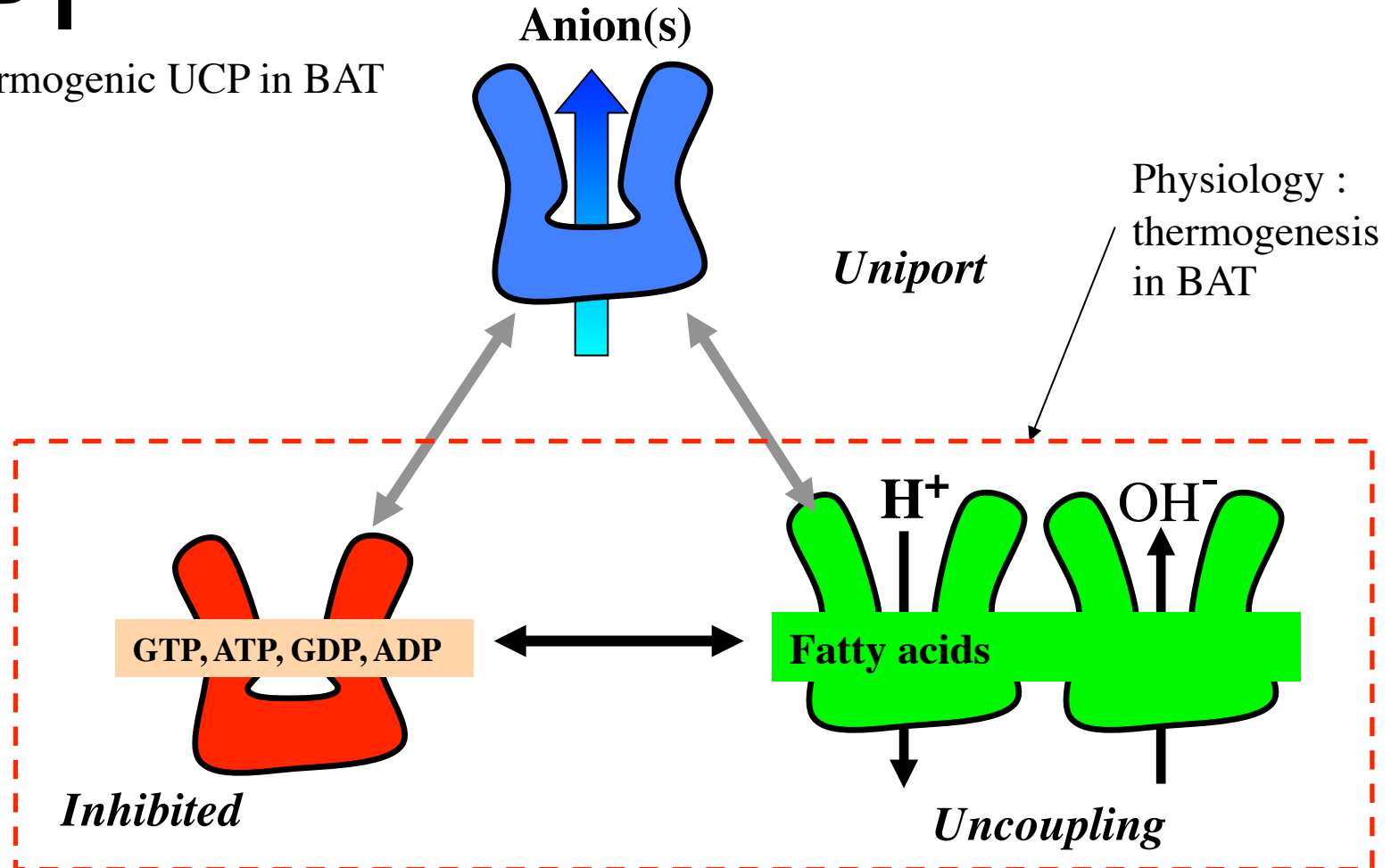
Physiol Rev • VOL 84 • JANUARY 2004 • www.prv.org

UnCoupling Protein 1 : UCP1



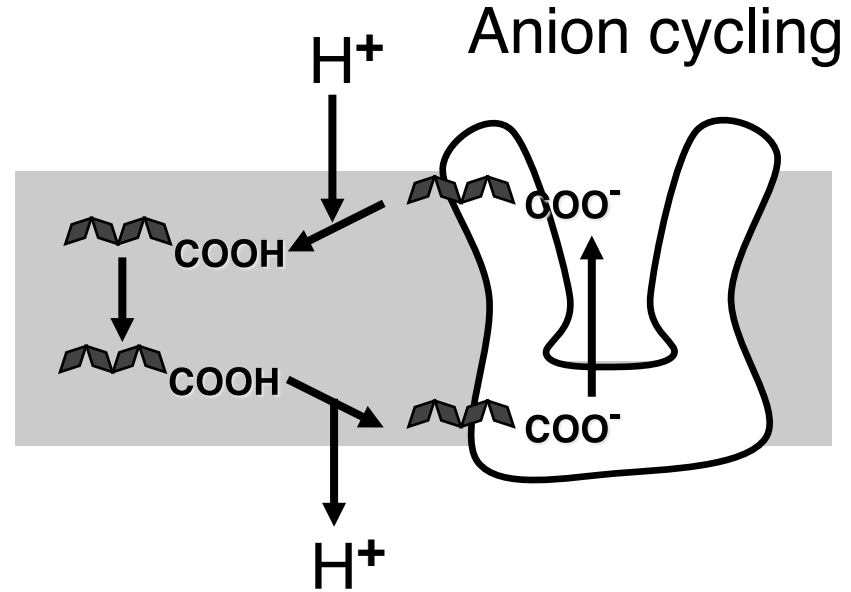
States of UCP1

UCP1 : thermogenic UCP in BAT

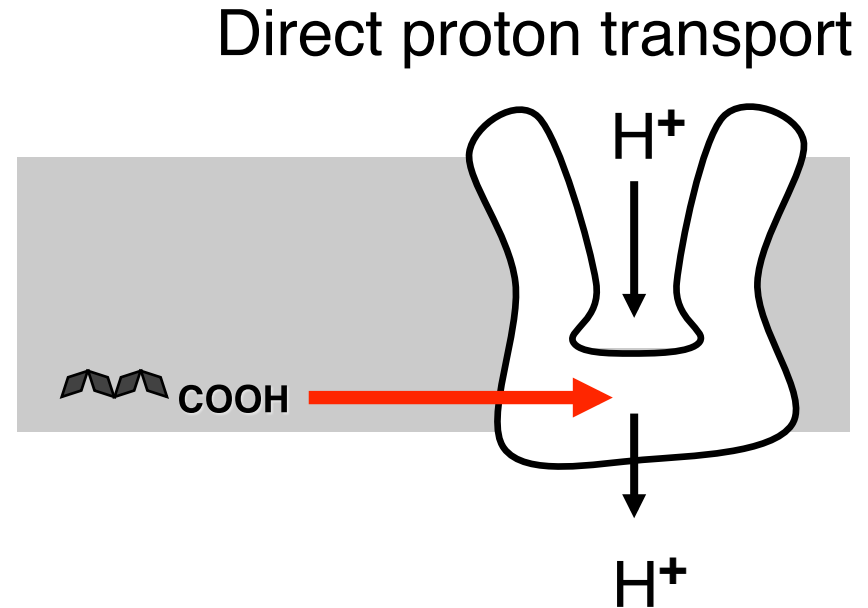


Modèles transport UCP

V. Skulachev
K. Garlid
...

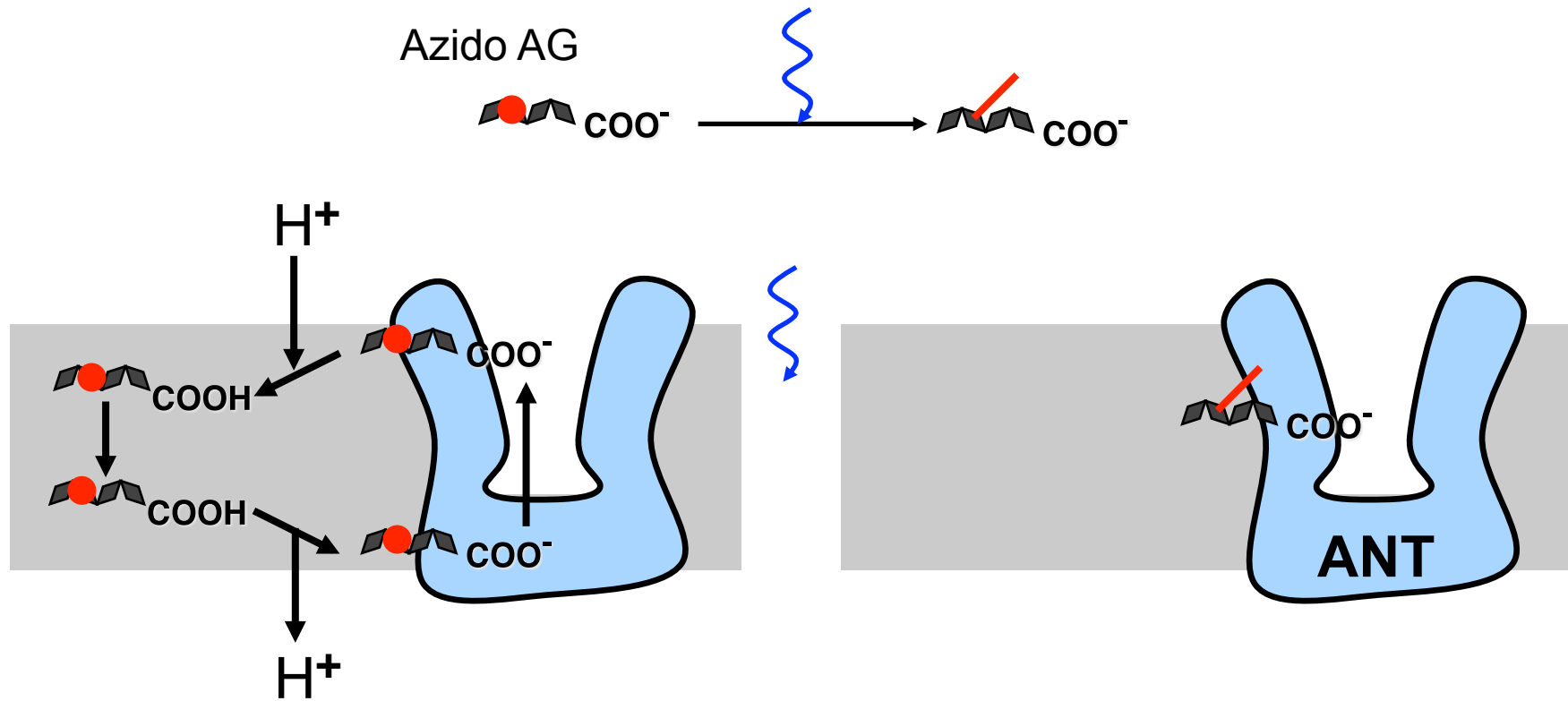


D. Nicholls
E. Rial
M. Klingenberg



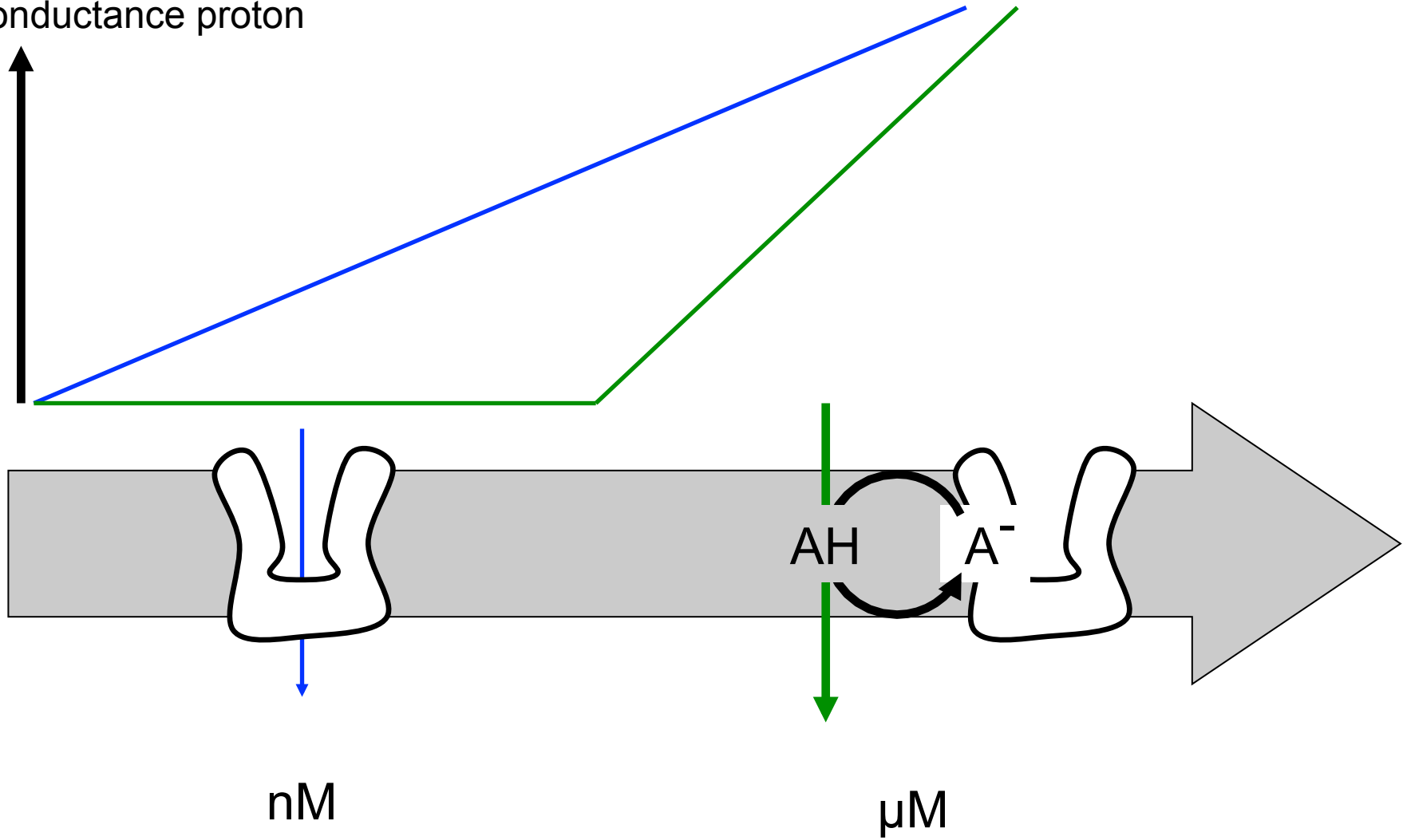
Une démonstration du cycle découplant des acides gras

P. Schönfeld



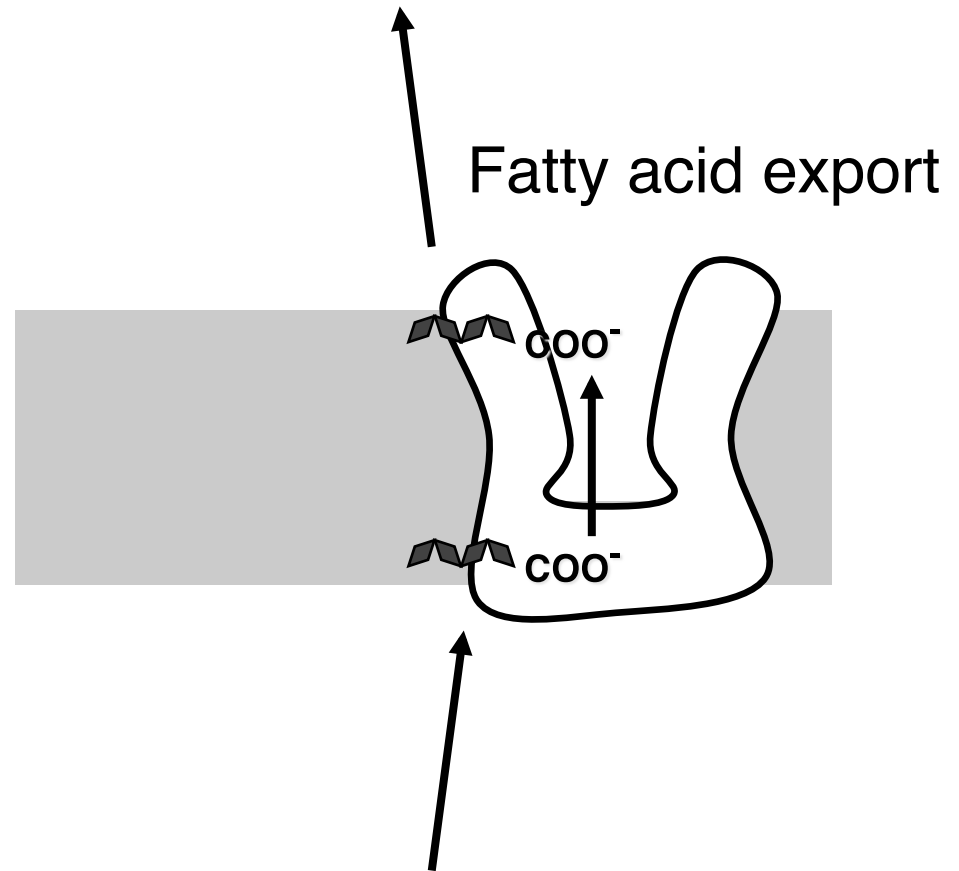
Un effet très dépendant de la concentration

Conductance proton



Fatty acid export out of mitochondria

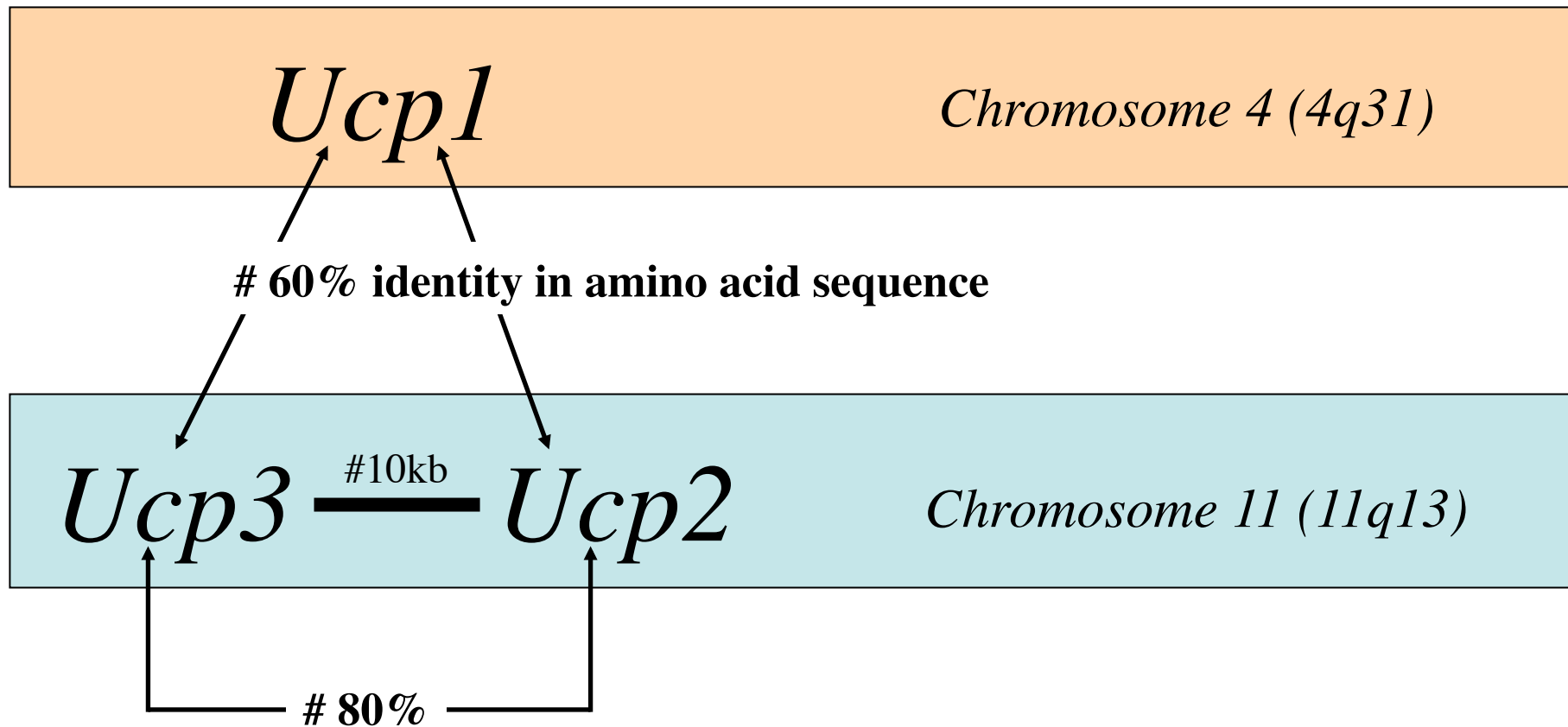
ME Harper
P. Schrauwen
...



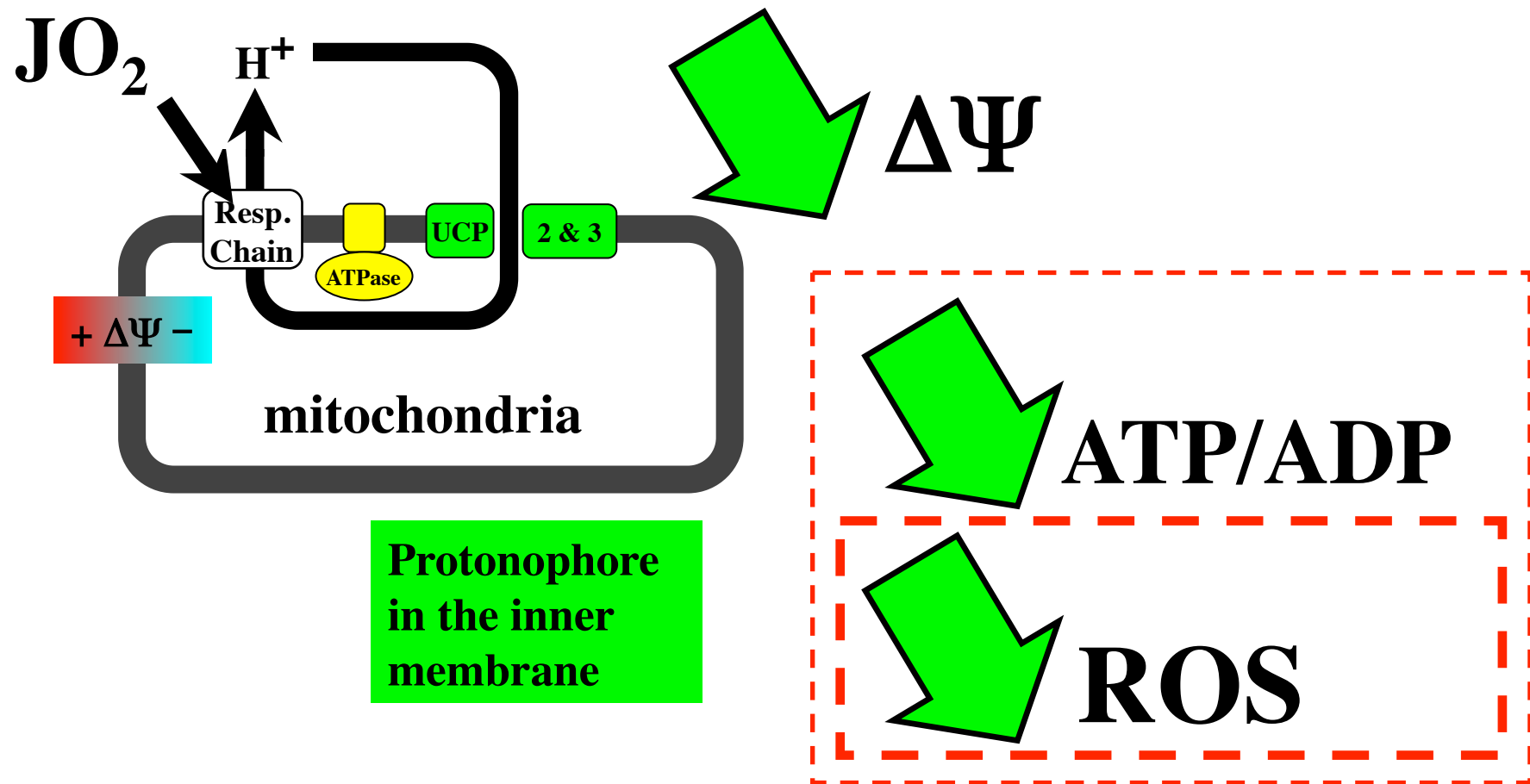
3) Les nouvelles UCPs

Nuclear genes

(chromosomal position in human)



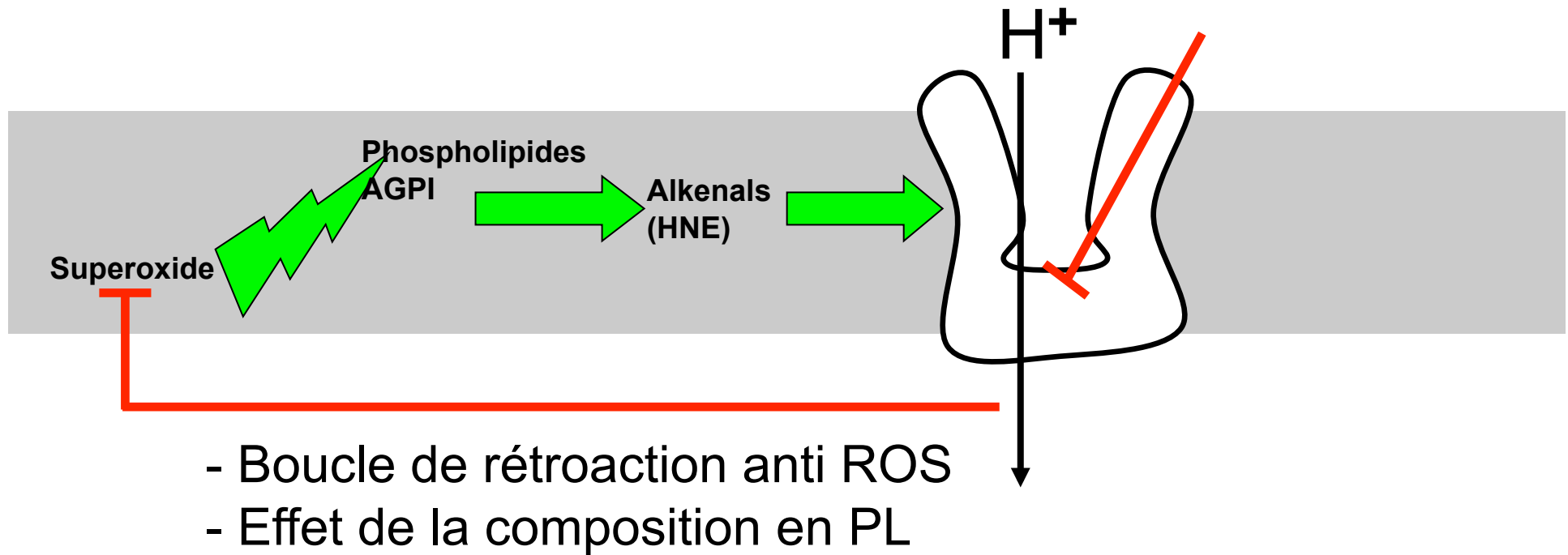
New UCPs (2,3, ...)



Superoxide activation of UCPs

K. Echtay, MP Murphy, MD Brand,

CAT = ANT
GDP = UCP

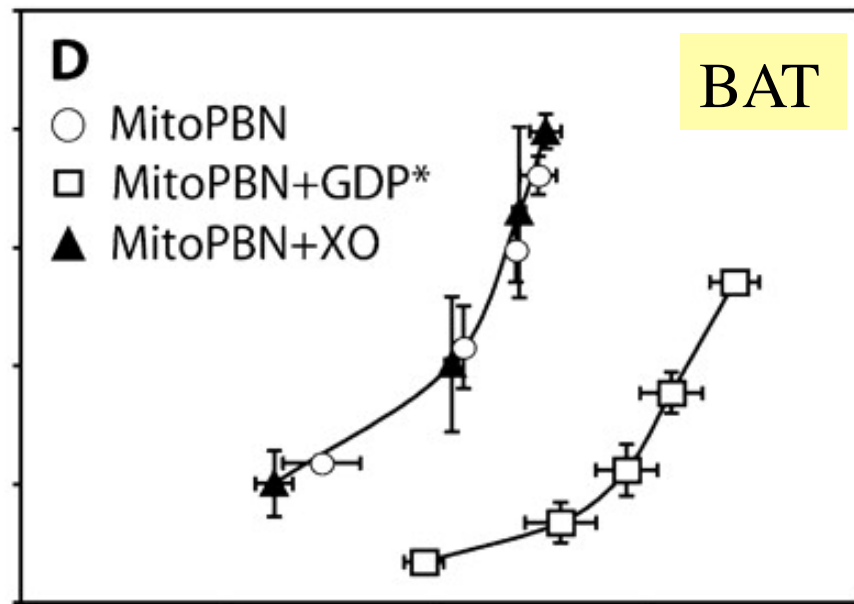
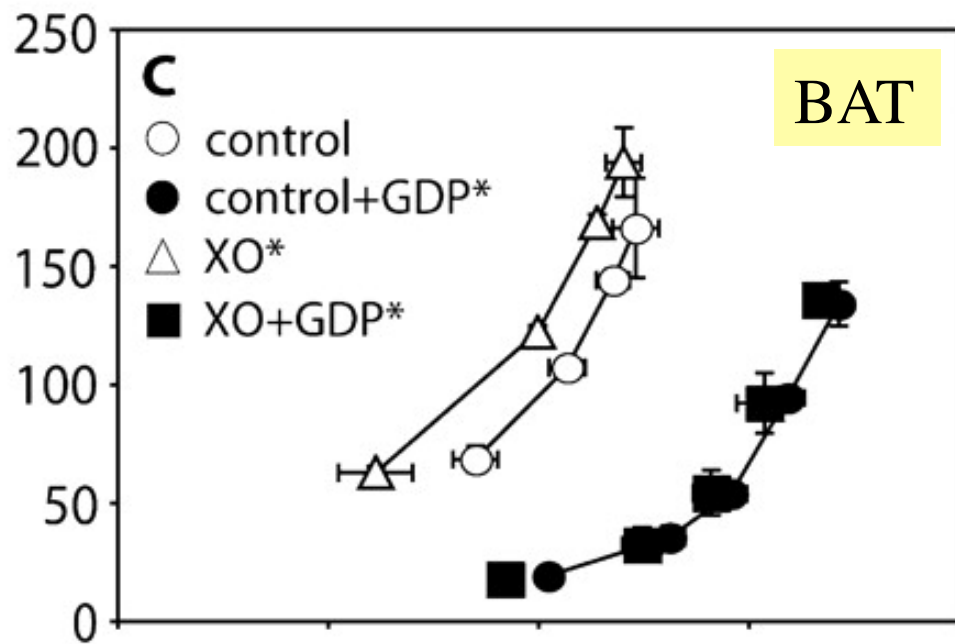
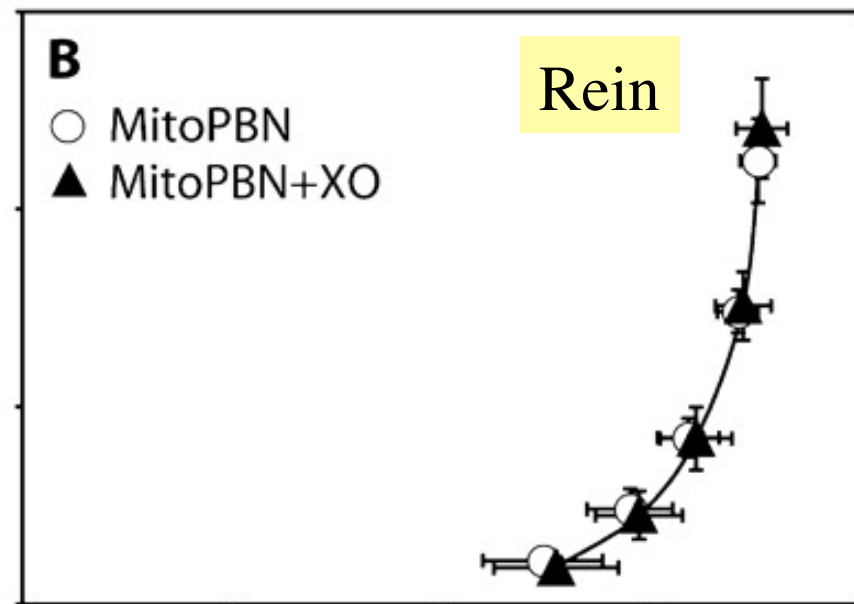
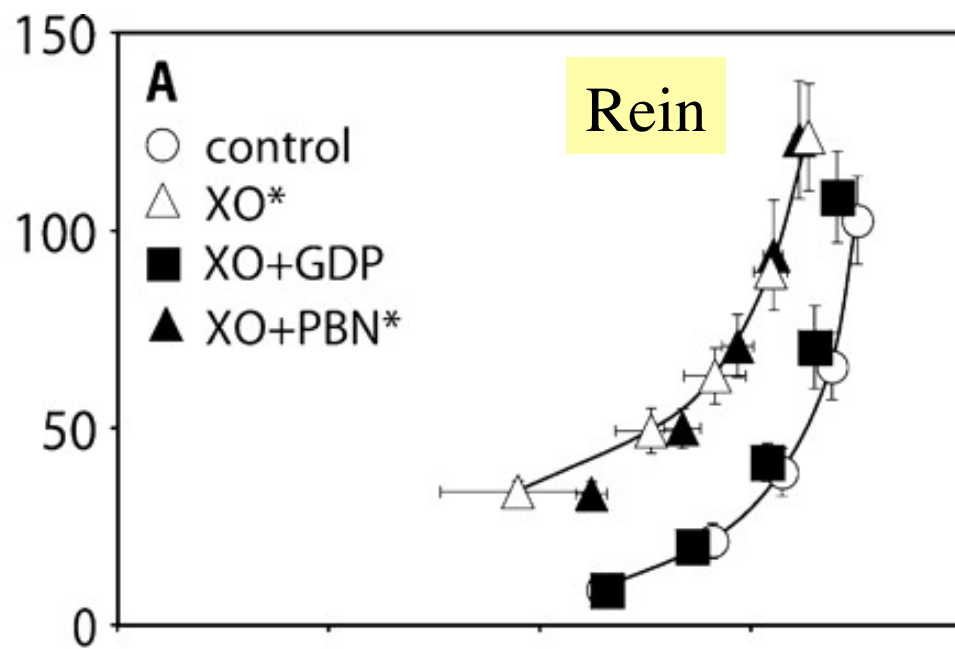


Inhibiteurs

Nucleotides

Genipin (UCP2 et secretion insuline)

B. Lowell



The basal proton conductance of mitochondria depends on adenine nucleotide translocase content

2005

Martin D. BRAND*^{1,2}, Julian L. PAKAY*, Augustine OCLLOO*, Jason KOKOSZKA†, Douglas C. WALLACE†³, Paul S. BROOKES‡⁴ and Emma J. CORNWALL*²

*Medical Research Council Dunn Human Nutrition Unit, Hills Road, Cambridge CB2 2XY, U.K., †Center for Mitochondrial Medicine, School of Public Health, Emory University, Atlanta, GA 30322, U.S.A., and ‡Department of Molecular and Cellular Pathology, University of Birmingham, Birmingham, AL 35294, U.S.A.

J Physiol 558.1 (2004) pp 123–135

Uncoupling protein and ATP/ADP carrier increase mitochondrial proton conductance after cold adaptation of king penguins

2004

Darren A. Talbot¹, Claude Duchamp², Benjamin Rey², Nicolas Hanuise², Jean Louis Rouanet², Brigitte Sibille² and Martin D. Brand¹

Carboxyatractylate-sensitive uncoupling in liver mitochondria from ground squirrels during hibernation and arousal

1990

N.N. Brustovetsky¹, Z.G. Amerkanov¹, M.E. Yegorova¹, E.N. Mokhova² and V.P. Skulachev²

Inhibitors of the ATP/ADP antiporter suppress stimulation of mitochondrial respiration and H⁺ permeability by palmitate and anionic detergents

N.N. Brustovetsky¹, V.I. Dedukhova², M.V. Egorova¹, E.N. Mokhova² and V.P. Skulachev²

Ce qu'il faut dire aussi

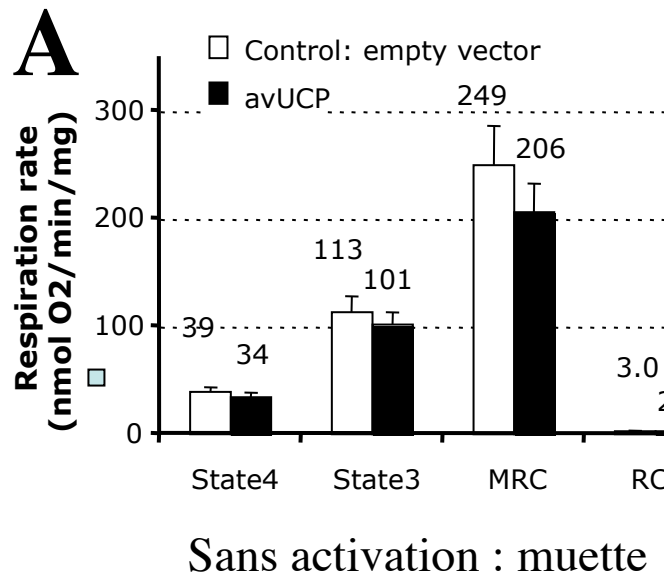
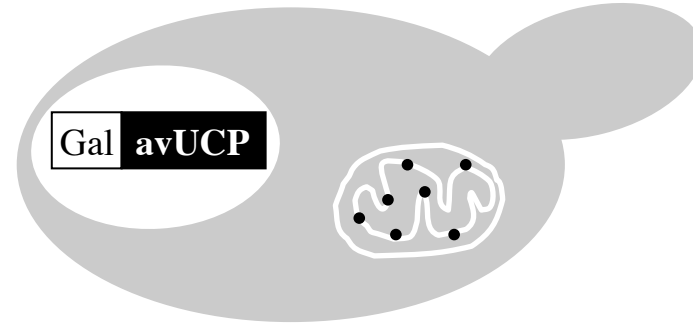
- La spécificité « UCP » est perdue
 - Le carrier le plus exprimé domine
- Une parade qui intervient après les dégats
- Physiologie « cellulaire »
 - Ce découplage est il intense (courbes très décalées)
 - Qui l'a vu ?
 - Ou bien très limité ?
 - Mais alors une consommation d'ATP un tout petit peu supérieure...
 - Une prédiction évidente est que en présence d'oligomycine cela conduit à l'apparition d'une voie découplante attribuable à UCP ou ANT... expérience encore attendue.



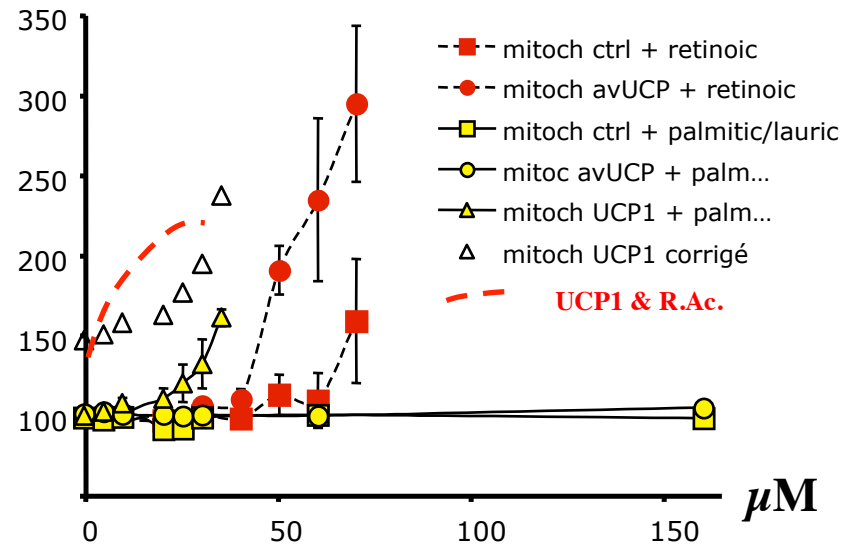
Pink ball - A resting flamingo in Hagenbecks Tierpark in Hamburg, Germany. The photographer, Vladimir Prassolov, is a professor at the Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia. His hobbies are bird watching and photography. This image won the first prize in the EMBO Journal's recent contest for the best non-scientific cover image for 2007.

Expression recombinante chez la levure de l'avUCP. *Criscuolo et al (2005).*

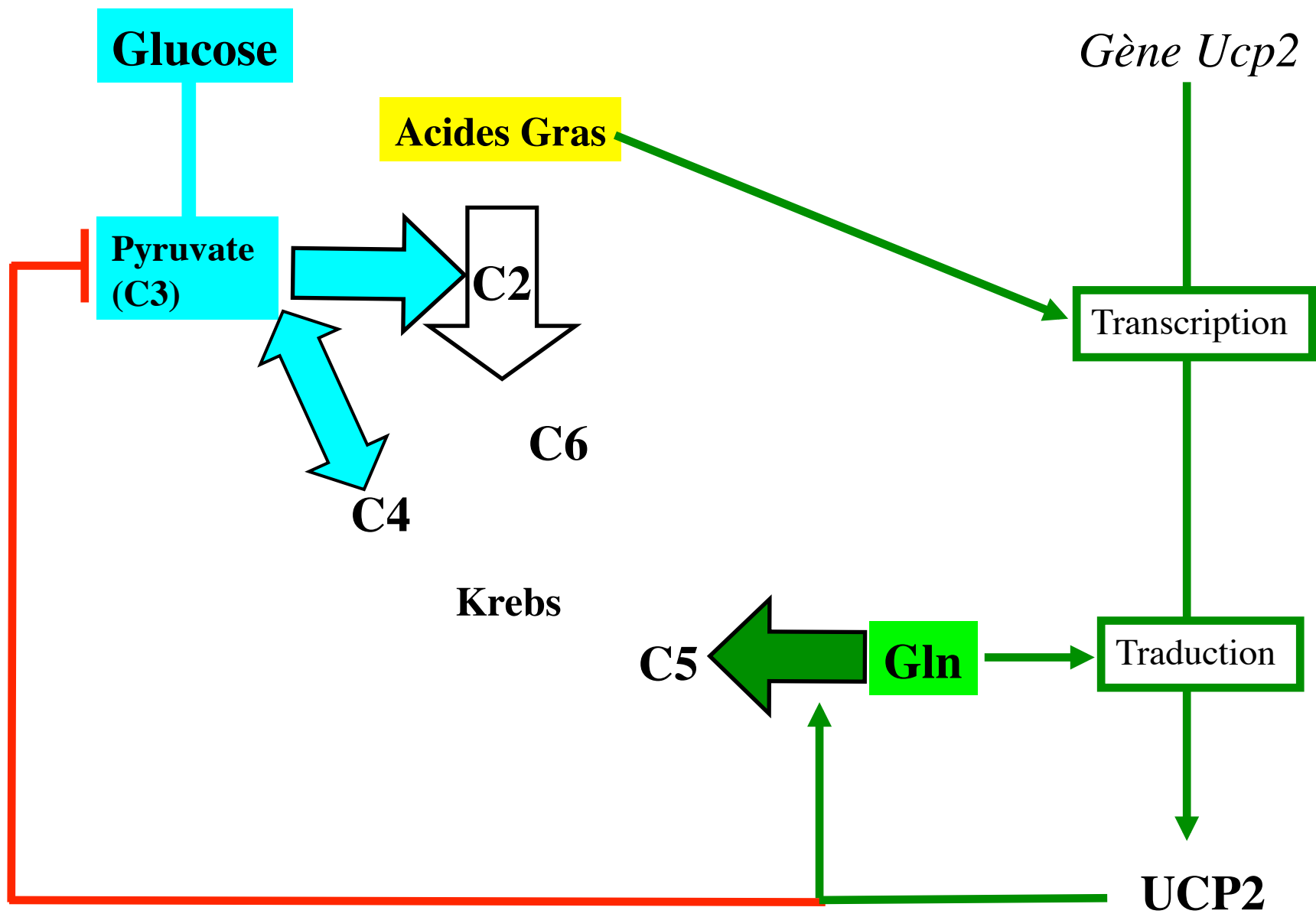
Birds	Mammals
-	UCP1
avUCP	UCP2
	UCP3



Stimulation %

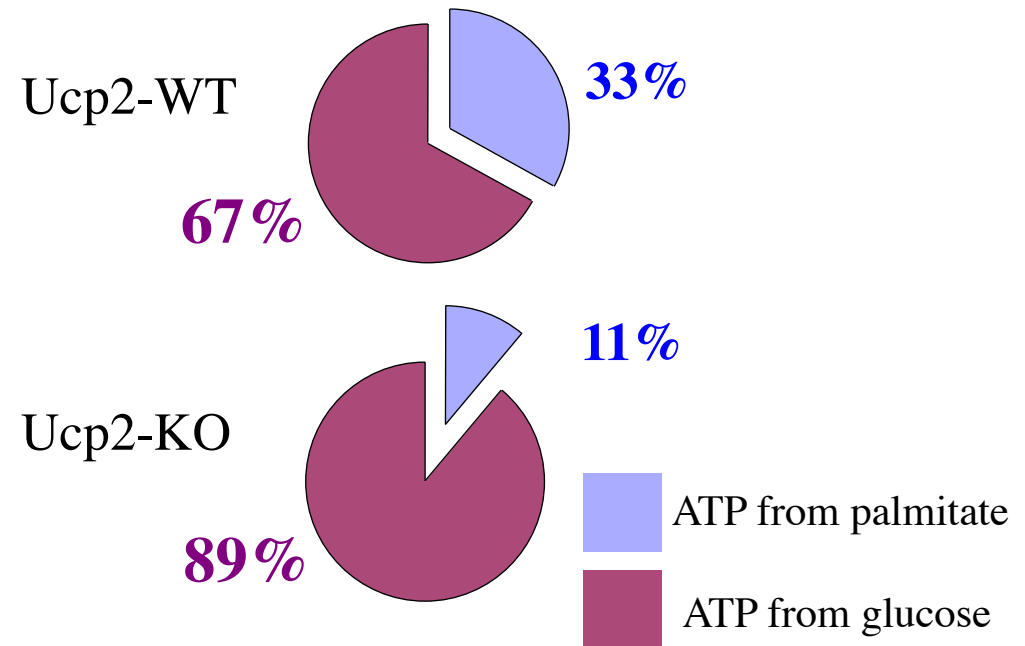
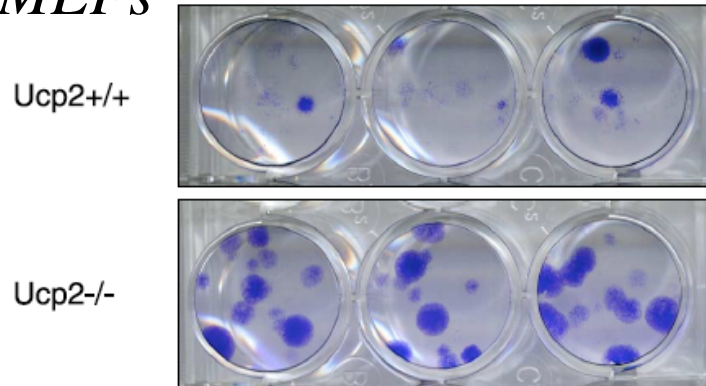


Activation bien réelle *in vitro*

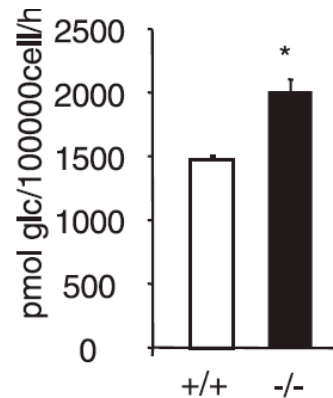


UCP2, division cellulaire et métabolisme, *Pecqueur et al (2007), FASEB J*

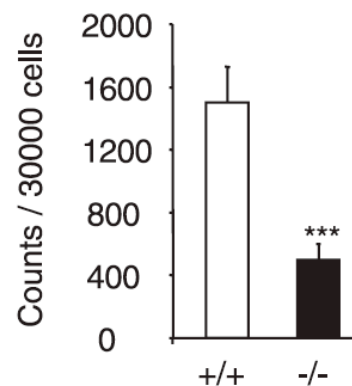
MEFs



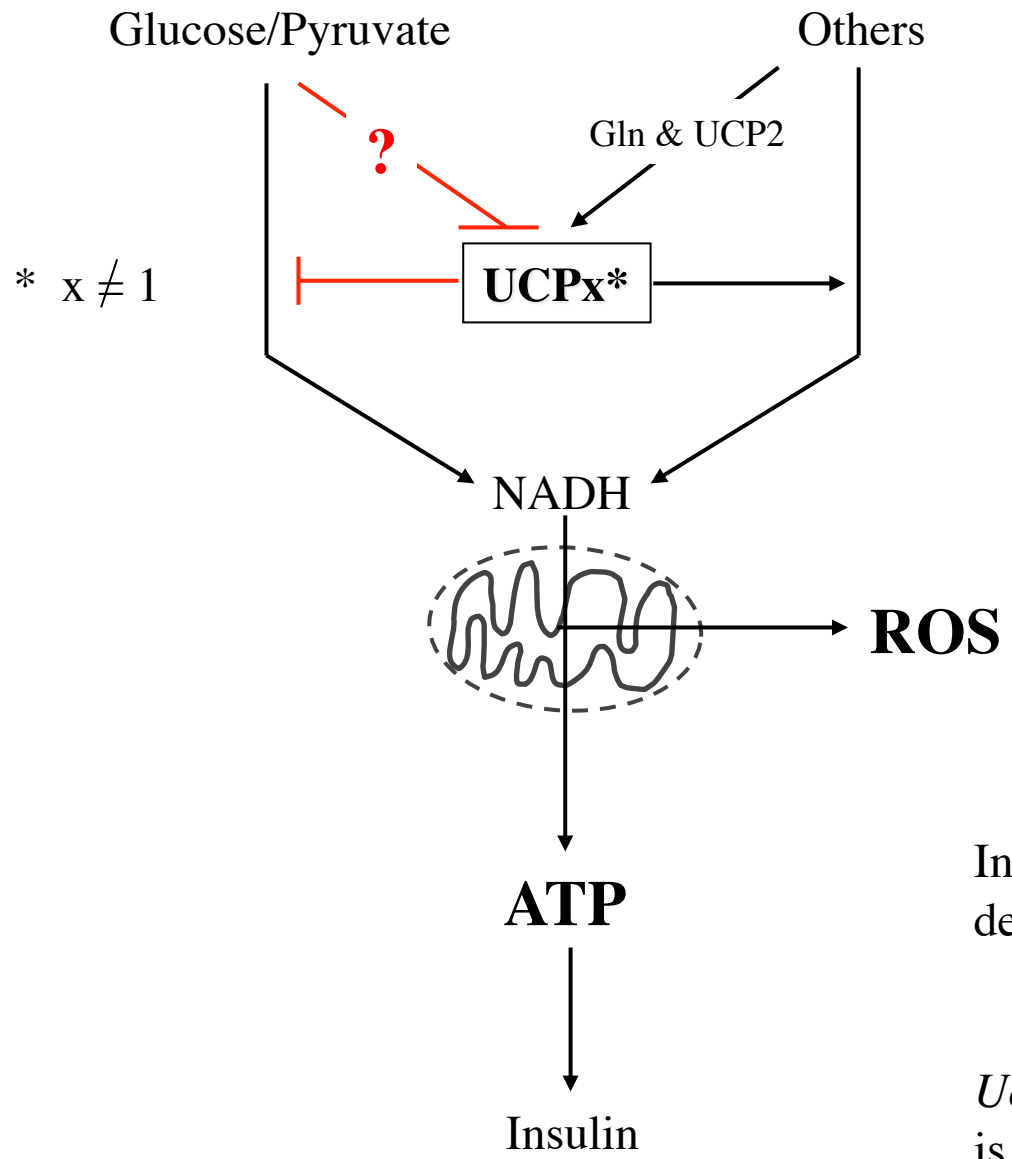
Oxyd. Glucose



Oxyd. Palmitate



La dépendance du rapport ATP/ADP au glucose est plus grande chez le KO. Toute signalisation (insuline) influencée par ce rapport est donc plus dépendante du glucose chez le KO.



More ROS in *Ucp2-KO*
2 entries of substrates

In presence of UCP2 ATP is less dependent on Glucose.

Ucp2-KO Insulinic response to glucose is enhanced